A STUDY OF FIBRINOGEN, PROTHROMBIN TIME, SERUM TRANSAMINASES IN NORMAL PREGNANCY AND PREECLAMPSIA AND THEIR SIGNIFICANCE AS A DIAGNOSTIC TOOL AMONG PREECLAMPSIA PATIENTS

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ABSTRACT

BACKGROUND

Preeclampsia is the important cause of perinatal mortality and morbidity. It causes marked deterioration in function of various organs and systems. Disseminated intravascular Coagulation (DIC) is a characteristic feature of PIH.

AIMS

The aim of the present study is to show the biochemical changes such as Fibrinogen, Prothrombin time, Serum Transaminases which occur in normal pregnancy and in preeclampsia and comparison with normal female subjects.

SETTINGS AND DESIGN

Prospective randomized case-control study.

METHODS AND MATERIAL

A total of 120 patients were selected for the testing of Fibrinogen, Prothrombin time and serum transaminase levels who were divided into three groups (40 patients in each group) for correlating the values of biochemical changes and to understand the significance between the groups. Graph pad Software was used for statistical Analysis.

RESULTS

Fibrinogen levels were higher in Normal pregnancy and preeclampsia group than Non-pregnant women. Significant prolongation of Prothrombin time was seen among preeclampsia group when compared with Non-pregnant women. SGOT and SGPT were elevated more in Preeclampsia group when compared to other two groups. The estimated variables (Fibrinogen, Prothrombin time, SGOT, SGPT) have shown that there is a good correlation of variables between non pregnant and preeclampsia groups and also normal pregnancy and preeclampsia groups which was statistically significant.

CONCLUSION

Detection of these changes in early period, can stop the progression towards Eclampsia and will be useful to start the appropriate treatment.

KEYWORDS

Fibrinogen, Prothrombin time, Serum Transaminases, Preeclampsia.

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INTRODUCTION: Hypertensive disorders in pregnancy plays an important role in perinatal mortality and morbidity. It usually appears after the 20th week of gestation. Pregnancy Induced Hypertension (PIH) includes a milder form of Preeclampsia and severe form of Eclampsia associated with convulsions, coma, hypertension. The rise in blood pressure may be quick or it may be gradual or subtle. Preeclampsia is a disorder of pregnancy characterized by high blood pressure and a large amount of protein in the urine. [1] Blood pressure is defined as high when it is greater than 140 mm Hg systolic or 90mm Hg diastolic at two separate times, more than four hours apart in a woman after twenty weeks of pregnancy. [2]

Hypertension is the predominant feature of the disease. Of all the signs the blood pressure is the earliest indication of the possible onset of the toxemias. It usually precedes albuminuria and even oedema also. Hypertension alone in the absence of proteinuria was associated with a three-fold rise in the foetal death rate (Diastolic >95mmHg).

Mild pre-eclampsia is defined as the presence of hypertension (BP ≥140/90mm Hg) on two occasions, at least 6 hours apart, but without evidence of end-organ damage, in a woman who was normotensive before 20 weeks gestation. Severe pre-eclampsia is defined as the presence of one of the

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following symptoms or signs: SBP ≥160 mmHg or DBP ≥110 mmHg on 2 occasions at least 6 hours apart or Proteinuria >5g in 24 hours urine sample or Pulmonary oedema or Oliguria or persistent headaches, or Epigastric pain or Thrombocytopenia or Oligohydramnios.

Preeclampsia affects approximately 4.5 to 11.2% of pregnancies in industrialized countries.[3] Although the specific cause of preeclampsia remains unknown, several factors contribute to the development of the disease spectrum, including the onset of vasospasm, activation of the coagulation system, Oxidative stressors, increased inflammatory response and ischemia.[4,5] Preeclampsia chiefly occurs in Primigravida (70%).

Main pathophysiology of preeclampsia is due to vasospasm. It is generally agreed that hypertension in preeclampsia is not neurogenic but essentially humoral in origin. Vasoconstriction causes increase in arterial hypertension. In PIH there is increased vascular reactivity to pressor hormones like angiotensin II or norepinephrine or vasopressin, which was demonstrated by Talledo et al [6] and Browne J et al. [7]

PIH occurs chiefly in primigravida and also in such conditions where there is reducing uteroplacental blood flow such as multiple pregnancy, obesity, diabetes mellitus, emotional stress, renal disorders. Usually occurs in the 3rd trimester of pregnancy, not common before 24th week.

Maternal consequences of PIH: Various organ functions will markedly deteriorated among pre-eclamptic patients. Disseminated intravascular Coagulation (DIC) is a characteristic feature of PIH. Thrombocytopenia infrequently severe, is the most frequent finding. The platelet count is below 1,50,000/mm3 in 26% of cases and below 1,00,000 in 15% of cases. Levels of fibrin degradation products in serum are clearly elevated. Angiotensin II, Renin, Aldosterone secretion usually diminishes. [8] Renal function tests are altered. Elevation of liver enzymes such as Serum Glutamic Oxaloacetic Transaminase (SGOT), serum alkaline phosphatase. Haemorrhagic necrosis in the periphery of liver lobule is the characteristic feature. Hypoxia will cause changes in placenta which results in changes in steroid hormones and gonadotrophins secretion, in turn leads to foetal hypoxia. In brain intense vasoconstriction and tissue hypoxia are presumably the cause of convulsions and coma.

The aim of the present study is to detect Fibrinogen, Prothrombin time, serum transaminase levels among Preeclampsia patients, normal pregnant and non-pregnant women and also comparing the biochemical changes among them. This topic was taken because of the more prevalence of Toxemias of pregnancy and there is a need for early diagnosis and to start early, appropriate treatment which halts the progression of preeclampsia to eclampsia.

MATERIALS AND METHODS: This is randomized case-control study done in Biochemistry department at Gandhi Medical College, Hyderabad. Ethical committee has approved and informed consent was taken from all patients.

A total of 120 patients were selected for the testing of Fibrinogen, Prothrombin time and serum transaminases levels.

120 patients were divided into three groups (40 patients in each group) for correlating the values of biochemical changes and to understand the significance between the groups. They were:

1. Preeclampsia group: Those subjects were showing the symptoms such as oedema, oliguria and high blood pressure greater than 140 mm Hg systolic or 90 mm Hg diastolic.
2. Normal pregnant group: Normal pregnant women without evidence of Hypertension, Diabetes, Renal disorders.
3. Normal non-pregnant group: Females who are married but not yet conceived were considered under this group.

Inclusion Criteria for Preeclampsia patients:

1. Patients did not have history of bleeding tendency.
2. Patients did not have previous history of hypertension, Diabetes.
3. Non-Alcoholic, Non-Smokers.
4. No evidence of liver, cardiac, renal, thyroid disease.

Blood samples were collected from patients and analyzed using following methods:

1. Estimation of Fibrinogen by Rapid Turbidimetric method.[9]
2. Estimation of Prothrombin time by One-stage Prothrombin time.[10]
3. Estimation of Serum Glutamic Oxaloacetic Transaminase and Serum Glutamic Pyruvic transaminase by Colorimetric method of Reitman & Frankel.[11]

After the estimation of these values, were analyzed, calculated.

Statistical Analysis: Statistical analysis was done using GraphPad software. A P value of <0.05 was considered significant.

RESULTS: Estimation of Fibrinogen, Prothrombin time, Serum transaminases levels done among 120 patients. All the values of fibrinogen, prothrombin time and serum transaminases (SGOT, SGPT) were tabulated by estimating mean along with standard deviation and were depicted in Table 1.

Fibrinogen levels were higher in Normal pregnancy and Preeclampsia group when compared to Non-pregnant women. There is significant prolongation of Prothrombin time among preeclampsia when compared with Non-pregnant women. SGOT and SGPT were elevated more in Preeclampsia group when compared to other two groups. All the estimated values were raised in Preeclampsia when compared to other groups.

Sl. No.	Biochemical changes	Non-pregnant (Mean±SD)	Normal pregnancy (Mean±SD)	Preeclampsia (Mean±SD)
1	Fibrinogen	280.2±46.9	381.75±60.3	402.3±23.1
2	Prothrombin time	16.7±0.77	17.1±0.98	17.8±1.11
3	SGOT	12.5±3.66	13.6±3.61	39.3±7.15
4	SGPT	10.3±2.87	11.4±3.22	30.5±6.34

Table 1: Levels of Fibrinogen, Prothrombin time, SGOT, SGPT among normal non-pregnant women, normal pregnant females, preeclampsia patients

n=40 in each group; SGOT-Serum Glutamic Oxaloacetic Transaminase; SGPT-Serum Glutamic Pyruvic transaminase; S.D-Standard Deviation.

Statistical significance has estimated between all three groups (non-pregnant women, Normal pregnancy subjects, Preeclampsia patients. All these were tabulated in Table No: 2, 3 and 4). The estimated variables (Fibrinogen, Prothrombin time, SGOT, SGPT) shown that there is a good correlation of variables between non pregnant and preeclampsia groups and also normal pregnancy and preeclampsia groups.

Sl. No.	Biochemical changes	t value	df	P value	Statistical significance
1	Fibrinogen	8.4074	78	less than 0.0001	ESS
2	Prothrombin time	2.0298	78	0.0458	SS
3	SGOT	1.3533	78	0.1799	NSS
4	SGPT	1.6129	78	0.1108	NSS

Table 2: Non-pregnant women vs Normal pregnancy women

ESS-Extremely Statistically Significant; SS-Statistically Significant; NSS-Not Statistically Significant.

Sl. No.	Biochemical changes	t value	df	P value	Statistical significance
1	Fibrinogen	14.7709	78	less than 0.0001	ESS
2	Prothrombin time	5.1498	78	less than 0.0001	ESS
3	SGOT	21.1020	78	less than 0.0001	ESS
4	SGPT	18.3575	78	less than 0.0001	ESS

Table 3: Non-pregnant women Vs Preeclampsia patients

ESS-Extremely Statistically Significant; SS-Statistically Significant; NSS-Not Statistically Significant.

Sl. No.	Biochemical changes	t value	df	P value	Statistical significance
1	Fibrinogen	2.0127	78	0.0476	SS
2	Prothrombin time	2.9899	78	0.0037	ESS
3	SGOT	20.2931	78	less than 0.0001	ESS
4	SGPT	16.9880	78	less than 0.0001	ESS

Table 4: Normal pregnancy women vs Preeclampsia patients

ESS-Extremely Statistically Significant; SS-Statistically Significant; NSS-Not Statistically Significant.

DISCUSSION: One of the most characteristic changes in severe preeclampsia is a fall in platelet count, [12] which may start from early in the disease process [13] and is probably explained by platelet consumption during low-grade intravascular coagulation. Disseminated intravascular coagulation is a characteristic feature of PIH and it plays a dominant role in the pathogenesis of the syndrome. In some cases of severe preeclampsia, however the disseminated intravascular coagulation can be sufficiently severe to precipitate micro-angiopathic haemolytic anaemia. [14]

Low or falling counts should always be taken as an indication of severe disease and it is important that clotting time and platelet count be performed in all cases of preeclampsia. In addition, there is evidence of thrombin activation in preeclampsia. [15]

Fibrin polymer complexes were higher in normal pregnant women than in nonpregnant controls but the levels were much higher in severe preeclampsia and these complexes are mainly dimers indicating thrombin activity. Fibrin degradation products are increased three times over those found in normal pregnancy [16] and those of urinary FDP are also markedly raised.

The release of transaminases from the damaged tissue and the significance of SGOT and SGPT as indices of cell death has been well documented. Liver changes are found in 60-70% of women dying of eclampsia and preeclampsia, and lesions have been found on biopsies of liver. The lesions are not specific to preeclampsia or eclampsia but are manifestations of vasoconstriction and disseminated intravascular coagulation.

In the present study the significant increase in fibrinogen levels in normal pregnant when compared to non-pregnant women, and there is lesser significance of increase in fibrinogen levels among preeclampsia when compared to normal pregnancy people. Agarwal et al [17] and Hakim et al [18] documented that fibrinogen levels have increased in normal pregnancy especially at term. Yusuf Ustun et al [19] found higher levels of Fibrinogen and CRP in Preeclampsia. Chatterjee T et al [20] has also reported that there is increase in Plasma Fibrinogen levels in Preeclampsia and Eclampsia about 70% and 145% respectively.

As per this study there was significant prolongation of Prothrombin time among preeclampsia when compared with Non-pregnant women and Normal Pregnancy. Alice Konijnenberg [21] observed that during preeclampsia there is a more extensively activated state of platelets while observing in Flow cytometric analysis when compared with

normal pregnancy. Priyanka Chauhan et al [22] reported that platelet count decreased significantly among preeclampsia and eclampsia and PT, aPTT, CT were normal but BT was prolonged.

SGOT and SGPT were elevated more in Preeclampsia group when compared to other two groups in this study. There was significant correlation of these values between preeclampsia and Non pregnant, Normal Pregnancy women but not between Non-pregnant and Normal Pregnancy women. Menzies J et al [23] documented that elevation of liver enzymes and creatinine levels were associated with adverse maternal outcomes in preeclamptic patients. Hazari NR et al [24] documented that there is an increase in SGOT, SGPT, ALP, GGT levels among Preeclampsia significantly whereas protein and albumin levels were decreased. Knox TA et al [25] stated that Aminotransferases and Lactate dehydrogenases leakage into maternal circulation is due to Oedema of the liver and hepatocellular necrosis.

CONCLUSION: From this study we conclude that there is increase in Fibrinogen levels, SGOT, SGPT and prolongation of Prothrombin time in Preeclamptic patients when compared with Normal Pregnancy and Non-pregnant women. Detection of these changes in early period, can stop the progression of eclampsia and will be useful to start the appropriate treatment.

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